IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS & INTERFERENCES

Appln. Serial No.: 10/666,366	Attorney Docket No.: 34506.143
Filing Date: September 19, 2003	Group Art Unit: 1652
Appellant(s): HUANG et al.	Examiner: Hutson, Richard D.

Title: **METHOD OF INACTIVATING RIBONUCLEASES AT HIGH TEMPERATURE**

REPLY BRIEF

Mail Stop: Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

On Appeal From Art Unit 1652
Examiner: Richard G. Hutson, Ph.D.

Joseph T. Leone, Esq.
DeWitt Ross & Stevens S.C.
2 East Mifflin Street, Suite 600
Madison, WI 53703-2865
Telephone: 608-255-8891
Facsimile: 608-252-9243
Attorney For Appellant

I certify that this paper is being electronically submitted to the U.S. Patent and Trademark Office via the EFS-Web system on the following date:

Signature: _____ **Date:** 4 AUG. 2009

ARGUMENT

Appellants respectfully traverse several of the Office's positions presented in the Examiner's Answer.

Appellants argued in their main Brief that there is no technological reason or motivation to combine the RNase inhibitor of Ambion with the RT-PCR reaction of Mizutani et al. because:

1. Ambion does not teach that RNases are known contaminants of all RNA preparations; and
2. Ambion does not identify RT-PCR as an assay in which RNase contamination is inherently a concern.

See first paragraph on page 8 through the second full paragraph on page 9 of Appellants' main Brief as filed.

The Office has stated in the Examiner's Answer that RNases are not known contaminants in RT-PCR reactions (see passage quoted below). The Office, however, has maintained that adding the RNase inhibitor of Ambion to the RT-PCR reaction of Mizutani et al. would be obvious because the benefits of doing so outweigh the costs (Examiner's Answer, p. 16, 1st full paragraph):

> Thus, while RNases may not be known as inherent contaminants in RT-PCR reactions, Ambion, Inc. teach that RNases are known contaminants in the laboratory and thus one of skill in the art would be so motivated to take minor additional measure to protect ones experiment, especially if the benefit far out ways the cost. [*sic*].

Appellants traverse the allegation that one of skill in the art would be motivated to take the additional measure of adding an RNase inhibitor because the benefits putatively outweigh the costs. RNase inhibitors were known well before the publication of the Mizutani et al. reference (1998). Yet, Mizutani et al. **do not** use RNase inhibitors in their RT-PCR reaction. Mizutani et al. thus do not support the Office's position that a practitioner in the art would be motivated to take the additional measure to add an RNase inhibitor. Rather, Mizutani et al. support the position that a practitioner in the art would **not** be motivated to take the additional measure to add an RNase inhibitor to an RT-PCR reaction.

RT-PCR reactions are notorious in the art for being fickle with respect to generating consistent results. Adding non-essential components (such as RNase inhibitors) to the reaction is

not recommended because it introduces one more variable that may cause the reaction to crash. The success of the Mizutani et al. RT-PCR reaction shows that RNase inhibitors are not essential to successful RT-PCR. Given the availability of RNase inhibitors at the time, Mizutani et al. further show that RNase inhibitors are not even preferred. The benefits of adding an RNase inhibitor do not outweigh the costs in Mizutani et al. - if that were the case, Mizutani et al. would have used one or more inhibitors in their reaction. The Office has not produced a reference wherein an RNase inhibitor was actually added to an RT-PCR reaction. If adding RNase inhibitor to an RT-PCR truly outweighed the potential risks of adding more reactants to the RT-PCR cocktail, this would have been common practice in the art at the time the Mizutani et al. paper was published. Mizutani et al., however, are completely silent with respect to RNase inhibitors.

Appellants thus submit that there is no technological reason or motivation to combine the RNase inhibitor of Ambion with the RT-PCR reaction of Mizutani et al.

Despite stating that RNases are not inherent contaminants in RT-PCR reactions, the Office has continued to rely on the contention that RNases "are known contaminants of RNA preparations" to justify the combination of Ambion with Mizutani et al. See, for example, the last four lines on page 9 of the Examiner's Answer. However, Ambion does not teach that RNases are known contaminants of RNA preparations any more than it teaches that that RNases are inherent contaminants in RT-PCR reactions. Ambion teaches only sources where RNase contamination **might** originate. Ambion does not teach or suggest that RNases are **known** contaminants of RNA preparations. It is improper to rely on such a contention to justify the combination of Ambion with Mizutani et al.

Appellants thus submit that Ambion and Mizutani et al. together fail to render obvious the present claims.

CONCLUSION

In light of the above arguments, the Board is therefore respectfully requested to reverse the only rejection now of record and to allow all of Claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40, and 42-45.

Respectfully submitted,

Joseph T. Leone, Esq., Registration No. 37,170
Daniel A. Blasiole, Ph.D., Registration No. 64,469
DeWitt Ross & Stevens S.C.
2 East Mifflin Street, Suite 600
Madison, WI 53703-2865
Telephone: 608-255-8891
Facsimile: 608-252-9243